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EDITORIAL

What Are the Benefits and Costs of Screening Mammograms on Kentucky Women Aged 40–49?

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The justification for mammographic screening for breast cancer in women in the 40- to 49-year age group remains dubious. One point of view is provided in Dodd's [1] editorial in the September issue of the Journal, with a commentary by Lawrence [2].

The National Cancer Institute (NCI) withdrew its endorsement of mammographic screening of women under 50 years of age in 1995 because of shaky supporting evidence and the very high cost [3]. This decision was called political by some, according to Lawrence [2]. An ethical objective of the political system is to ensure that the benefit of public health programs is confirmed by good science and the attainment of the benefit is achieved at a cost society can afford. The recommendation of the Director of the NCI to withdraw NCI support for screening mammograms among women aged 40–49 was a politically responsible act. The Kentucky Health Policy Board (KHPB), authorized by the Kentucky General Assembly in 1994, has also had to grapple with the political and economic realities of breast cancer screening.

Whether to perform screening mammograms on Kentucky women aged 40–49 has proved a disputed issue before the KHPB, created by Kentucky Health Care Reform Bill House Bill 250 (HB). The KHPB may adopt guidelines developed by the Agency for Health Care Policy and Research. It may also adopt parameters developed by other qualified bodies, or it may develop its own practice parameters with the help of intrastate advisory groups.

Ongoing evaluation of practice parameters is authorized. The parameters are to be disseminated to professional licensing bodies. Various outcome measurements are to be developed and disseminated to various regulatory bodies. The practice parameters are to be periodically updated on the basis of data collected from the implementation of these parameters. The KHPB is to recommend implementation of the parameters for use by health care providers and provide continuing education of the parameters to providers. The breast cancer screening advisory committee's position is that the cost of parameters must be justified in competing for an equitable share of the health dollar and proved effective by population-based controlled clinical trials. The fact that infinite resources are not available for health care has become obvious to all. The issue is not that the health dollar should not be rationed. For the physician to remain the patients' advocate, the primary issue is not to sanction rationing but to determine how to spend the health care dollar most effectively through the adoption of practice parameters of proven value. Anecdotal case reports were not considered a substitute for controlled clinical trials. In this process there must be recognition of large expenditures with no or even negative benefit. The national pressure for mammography extends to Kentucky. The purpose of this editorial is to consider the costs and benefits of a rational program for Kentucky women.

In Kentucky, breast cancer afflicts approximately 2,400 women each year, and 610 of them are estimated to die of it annually. The accuracy of these estimates is not known [4]. About 70% of adult women have some form of chronic cystic changes [5], now classified as aberrations of normal development and involution of the breast

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[6], that produce symptoms and signs requiring evaluation and treatment. Only a small subset (4%) of the latter conditions are associated with a statistically significant increase in the relative risk of future development of breast cancer [5], but all breast symptoms and signs require complete evaluation and a plan for management, beyond screening with counseling. Most breast cancers occur in women with no recognized antecedent risk factors [7].

House Bill 250 created the KHPB with broad obligations and authority. It is charged to control health care costs, improve the quality and efficiency of health care, encourage competition, and develop a "system of integrated health care delivery which makes necessary health services available to all residents of the Commonwealth." Each member of KHPB shall have demonstrated interest in the provision of efficient, economical, and quality health care. The board is charged with the obligation to reduce the rate of increase in total state health expenditures by 10% per year until the rate of increase equals that of the rate of increase in state personal income. To carry out its mission, various advisory committees are authorized to develop and monitor practice parameters. One committee is charged with the obligation to recommend screening parameters for breast cancer. The 2,400 new breast cancers are diagnosed predominantly among the 970,604 women over 35 years of age [8]. The residual lifetime probability of acquiring breast cancer declines past age 35 years, although the age-specific annual incidence rate steadily increases [9]. The age-adjusted probability of dying of breast cancer has not declined since the onset of adequate data collection in 1930. The annual age-adjusted death rates, according to race and age, are shown in Table I [10,11].

The lifetime risk of acquiring breast cancer is affected by family history [5]. However, less than 4% of women have a statistically significant family history, and then only when it is associated with hyperplasia and atypia. To reiterate, more than 80% of all breast cancers occur in women with no recognized antecedent risk factors [7]. To date, there is no intervention strategy of proven value for reducing the risk of dying of breast cancer once it is identified, and efforts to find an approach that will reduce risk is a subject of ongoing research. Now, any effective breast cancer control program must address the needs of all adult women.

INITIAL ASSESSMENT

In Kentucky, 153,198 women aged 35–39 are no longer considered a target for screening mammograms. There is little disagreement on the benefit of screening women aged 50–69 (661,580 women), although the optimum interval between mammograms merits further study. For many cancers, routine physical examination is as effective as mammography with respect to survivorship. Many breast cancers are not diagnosable on mammograms, and mammograms cannot be used to rule out cancer in the presence of positive physical findings. Thus, there is no disagreement regarding the need for periodic physical breast examinations (PBE), which may also discover benign disorders that may benefit from management. Breast self-examination (BSE), practiced monthly, leads to the discovery of some breast cancers at an average size of 2.1 cm, not a small cancer [12]. Controlled clinical trials on BSE have not confirmed it to be very effective in reducing mortality from breast cancer. Cancers discovered by BSE give a little lead time but show no improvement in survival [12].

The major disagreement on screening guidelines is related to screening mammograms in women aged 40–49. In Kentucky, there are 256,540 women in that age group, and the following data and calculations are relevant to assessing the costs and logistics of a screening program [8].

In Jefferson County, Kentucky, the cost of a screening mammogram ranges from $50 to $150: at $50/mammogram: 256,540 × $50 = $12,827,000 per year; at $150/mammogram: 256,540 × $150 = $38,481,000 per year. The total costs for taking and reading additional views and the arborizing costs of interventions associated with the nonbeneficial pursuit of false-positive readings is very large, but exact figures are not available.

The following data for Kentucky were abstracted from Cancer Facts and Figures—1994 [4]. The 30-year trend in breast cancer death rates in Kentucky for 1959–1961 was 25.8/100,000, and for 1989–1991 it was 27.4/100,000. The annual number of new breast cancers in Kentucky was 2,400; the annual number of deaths from breast cancer in Kentucky was 610. The mortality rate of breast cancer (assuming that all 610 with breast cancer did indeed die of it), is 610/2400 (25%).

The implications are that completely controlling all breast cancer would save 610 women from dying of breast cancer. About 30% of these women would be 40–49 years of age. One hundred eighty-three women, constituting 30% of the 610 total, might be saved from dying of breast cancer were mammography the first step in a completely effective cancer control program.

If all new breast cancers in Kentucky were discovered in Kentucky women aged 40–49, the cost per lethal cancer found, assuming 100% effectiveness for discovery by mammography, would be as follows:

At $50/mammogram 12,827,000 ÷ 183 = $70,093
At $150/mammogram 38,481,000 ÷ 183 = $210,279

Both the false-negative reading of mammograms and the interval surfacing of cancer in the 40- to 49-year age group is quite high and will vary with the quality of the

TABLE I. Death Rates for Malignant Neoplasm of Breast for Females, According to Race and Age

Race/Age (yr)	Selected years				
	1951	1960	1970	1980	1990
White					
All ages, age adjusted	22.5	22.4	23.4	22.8	22.9
All ages, crude	25.7	27.2	29.9	32.3	35.9
<25	0.1[a]	0.0[a]	0.0[a]	0.0[a]	0.0[a]
25–34	3.7	3.7	3.7	3.0	2.6
35–44	20.8	20.2	20.2	17.3	17.1
45–54	47.1	53.0	53.0	48.1	44.3
55–64	70.9	79.3	79.3	81.3	78.5
65–74	96.3	95.9	95.9	103.7	113.3
75–84	143.6	129.6	129.6	128.4	148.2
≥85	204.2	161.9	161.9	171.7	198.0
Black					
All ages, age adjusted	19.3	21.3	21.5	23.3	27.5
All ages, crude	16.4	18.7	19.7	22.9	29.0
<25	0.1[a]	0.2[a]	0.1[a]	0.0[a]	0.1[a]
25–34	4.9	6.1	5.9	5.3	5.3
35–44	21.0	24.8	24.4	24.1	25.8
45–54	46.5	54.4	52.0	52.7	60.5
55–64	64.3	63.2	64.7	79.9	93.1
65–74	67.0	72.3	77.3	84.3	112.2
75–84	—	87.5	101.8	114.1	140.5
≥85	—	92.1	112.1	149.9	201.5

[a]Based on fewer than 20 cases.
From Spratt [11].

mammography and the capacity of the cancer to image on mammograms. This means that significantly fewer cancers would be discovered by screening mammograms in this age group, and the true cost per lethal cancer found would be greater than these estimates.

As Kopans [13] observed, no existing controlled clinical trials of screening mammography had enough statistical power in numbers to detect a statistically significant reduction in breast cancer mortality in the 40- to 49-year age group.

This high cost has justified the performance of a number of controlled clinical trials on the efficacy of screening mammograms in women aged 40–49 years. Controlled clinical trials of mammography in this age group have reported results ranging from slight benefit to no benefit; in some trials, the group having mammograms had more breast cancer-related lethality than was found in the control groups [14,15]. Kopans [13] has been a proponent of ignoring the controlled clinical trials and proceeding with mammograms in the 40- to 49-year age group, arguing that the very fact that controlled clinical trials would require 500,000 women to determine whether mammography provides significant benefit, if any, establishes that the benefit would be exceedingly small. Kopans states, "The smaller the expected benefit, the larger the number of women needed in the trial, or, conversely, if the number of women in the trial is small, only a very large benefit can be demonstrated to be statistically significant." The trials described in Kopans's article involved 45,000 to 50,000 women. Because breast cancer is statistically a rare occurrence, differences would only be significant with this size sample if the mortality reduction rate was over 30% in the screened group. Anything less cannot be statistically significant. The result of increasing the size of the study sample to 500,000 would be to reduce the size of the mortality difference that would be statistically significant.

At this point, it must be considered that what is statistically significant may not be attainable. With a large enough sample, 0.5% reduction could be significant, but does such a low yield warrant mass screenings? Although the number 500,000 is given, the expected size of difference is not. Without that information, the number 500,000 is meaningless statistically.

To calculate what Kopans's recommendations would mean for Kentucky, Massachusetts General Hospital (MGH), where Kopans works, was contacted to obtain mammogram prices (Table II). Were MGH charges prevalent in Kentucky, the total annual cost of screening mammograms on women aged 40–49 would range from $67,726,560 to $97,228,660. Dividing by 183 results in $370,090.49 to $531,304.15 per potentially lethal cancer found by screening mammography in women aged 40–49. This again does not include costs of interventions for

TABLE II. Cost of Screening Mammograms at Massachusetts General Hospital*

Mammograms		Additional	Charges for	
Unilateral	Bilateral	views	reading	Range
$225	$250	$69	$39–60	$264–379

*Data obtained directly from Massachusetts General Hospital.

false-positive results, nor does it allow for cancers that surface in the intervals between mammograms or for false-negative mammograms.

Confronted with these data, a logical question to ask is, what is the real risk of acquiring breast cancer? The widely quoted statistic of 1:9 chance of the development of breast cancer is the accumulative probability of developing breast cancer between birth and age 110 years. Seidman et al. [9] provide the lifetime residual risk of dying of breast cancer at various ages. This risk declines with age even though the incidence slowly increases, but permits a more realistic assessment of risk than the 1:8 or 1:9 often quoted.

With this discussion as background, the following guidelines developed by the U.S. Preventive Services Task Group seemed acceptable and were recommended to the KHPB (Table III). The recommended baseline and annual mammograms for women aged 45–49 was not unanimously endorsed, as the same survival benefit may be obtained by a baseline mammogram at age 50.

The next question concerns what to do in the presence of positive findings on mammographic or physical examination. The discussion of this, with algorithms, is covered in the chapter entitled, "Diagnosis," in Donegan and Spratt's book [16].

There are 15,986,000 women aged 40–49 in the United States [10]. If Kopans's system and charges applied to all these women, the costs would range from $4,220,304,000 to $6,058,694,000 annually, plus the high cost of interventions for false-positive diagnoses made on mammograms. According to Kopans [13], 28,900 women aged 40–49 are diagnosed with breast cancer annually. By dividing 28,900 into the range of costs for the Kopans method of screening all 40- to 49-year-old American women, the cost per cancer found can be estimated as follows:

$$\$4,220,304,000 \div 28,900 = \$146,031$$
$$\$6,058,695,000 \div 28,900 = \$209,643$$

These costs are before any intervention for false-positive results or treatment for true-positives results begin. Furthermore, these costs do not allow for cancers not visible on mammograms nor cancers that surface in the intervals between annual mammograms.

According to data provided in Health United States 1994 [10], the use of mammography for women over age 50 during the preceding 2 years was 72.5% for women with more than 13 years of education and 46.9% for women with less than 12 years of education, a distinct increase, but still seemingly an elitist test for the well educated. No data were provided for women under 50 years of age.

To show a difference with sufficient power, Kopans contends, would require a sample of 500,000 women followed for many years, perhaps 10. By multiplying the MGH charges by 500,000, the first year cost would range from $132,000,000 to $189,500,000. Annual repetition over 10 years would reach $1,320,000,000–$1,895,000,000, plus the additional cost of interventions for false-positive diagnoses. An argument presented at the KHPB was the cost of failure to control a breast cancer after primary diagnosis exceeded the cost of discovery by screening. That argument does not counter the conclusion of most clinical trials that the trials diagnosing breast cancer as early as possible in women aged 40–49 still do not lead to a reduction in the probability of dying of breast cancer. Assessment of risk factors, most of which are not statistically significant, and attempts to use these assessments to improve the efficiency of screening have proved of limited value [17].

Eddy [18] noted that no one has ever surveyed women who have been fully informed regarding "benefits, harms, and costs," of mammographic screening so that their personal history and preferences are considered in their choices. For the less well-to-do, choices for the total expenditure of available health dollars and overall needs would be expected to influence decisions. Efforts promoting mammography of all women aged 40–49 should take this reality into account.

With the knowledge at hand on the potential for prevention, clearly some of the enormous amounts of money required to support mammography for women aged 40–49 as a growth industry should be redirected to prevention trials, as suggested by Colditz and Frazier [19].

The conclusions of Colditz and colleagues [19,20] are based on a mathematical model of the cause of breast cancer, originally conceived by Pike et al. [21], using data from the nurses' health study. The model identifies the year of first giving birth as the most crucial factor in determining the future risk of breast cancer. Other reproductive risk factors are considered and ranked. Pike noted that no more than 10–15% of breast cancer risk is inherited. Their conclusions were that population-based prevention activity would promote increased physical activity among young girls to delay the menarche. Other modifiable lifestyle factors are identified, as are specific life style changes with the potential for reducing the magnitude of the breast cancer epidemic. A recent tabula-

TABLE III. Screening for Breast Cancer in Kentucky Women

Screening examination	Age			
	19–39 yr	40–49 yr	50–74 yr	≥74 yr
BSE	Monthly	Monthly	Monthly	Physician and informed patient's judgment
PBE	Physician and informed patient's judgment	Yearly	Yearly	Physician and informed patient's judgment
Mammography	Not recommended	Only if at risk[a]	Every 2 yr at age 50; every 2 yr at ages 65–74	None

BSE, breast self-examination; PBE, physical breast examination.
[a]No clear definition of risk was agreed on.

tion of age-adjusted death rates for white and black females documents that these rates have not declined since 1950 and are increasing at 1.8–1.9% annually [10,11]. An illusion of improvement occurs when anatomic stage-specific fixed end-point (5- and 10-year) survival rates are reported in clinical series. Unfortunately, this method of reporting survivorship is subject to biases in assumption with respect to the staging system, length bias sampling, and lead time bias when relating anatomical (TNM) stages to the fixed end-point rates [11]. Furthermore, in analyzing reports from major clinical trials, Haybittle [22] observed that no trial had ever reported a statistical cure of invasive breast cancer. A statistical cure may be concluded when the force of mortality after therapeutic intervention parallels the expected force of mortality in the population with no breast cancer. These depressing facts alone mandate serious consideration of prevention trials.

CONCLUSION

There is a need for a comprehensive breast cancer control program in Kentucky. Screening for asymptomatic cancer is one component of a control program. Its high cost requires continued monitoring of benefit, as mandated by Kentucky HB 250. The objective is to ensure maximum benefit for all Kentucky women. The recommended screening parameters contained in Table III impose numerous costs in training manpower and upgrading quality of mammographic equipment and technique as an initial investment of unknown magnitude.

Overpromotion of the idea that widespread use of mammography will significantly reduce the risk of dying of breast cancer has led to many medicolegal actions. The frequency of these problems was recently reviewed at a Harvard Continuing Medical Education Conference held in Cambridge, Massachusetts (Sept. 22–23, 1995). An admonition from one speaker, S.H. Mackauf, attorney (Gair, Gair, Conason, Steigman & Mackauf, New York, NY), strikes at the heart of the medical legal issues. He stated in a private conversation with W. Steve Aaron, M.D. (Louisville, KY) that as long as doctors keep using mammography to "rule out breast cancer" in women with symptoms or physical findings and hold to the Halstedian misconception of breast cancer progression, he (Mackauf) will continue to win suits against the doctors for alleged delay in diagnosis of breast cancer. The general failure to control the epidemic of breast cancer with contemporary interventions must be confronted. The time for prevention trials may be at hand.

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